



Reports of Two Human Infections with Swine Origin Influenza A (H3N2) Viruses Showing Genetic Reassortment with 2009 H1N1 Virus.

Summary

- On September 2, 2011 a Morbidity and Mortality Report (MMWR) Early Release was issued entitled "Swine-Origin Influenza A (H3N2) Virus Infection in Two Children – Indiana and Pennsylvania, July-August, 2011."
- The article is available at <http://www.cdc.gov/mmwr/>.
- The MMWR details two reports of human infection with swine-origin triple-reassortant (tr) influenza A (H3N2) virus reported to CDC: one by the state of Indiana and another by Pennsylvania.
- These cases of swine-origin triple reassortant influenza are not epidemiologically linked.
- In both cases, there appears to be direct or indirect contact with swine.
- Investigations are ongoing in both states.
- Swine influenza A (H3N2) viruses normally infect pigs. These viruses rarely infect humans. However, human infections have occurred, usually following exposure to infected pigs.
- Genetic sequencing of both viruses has shown a genetic variation.
- This change is the acquisition of the Matrix gene, or "M" gene, from the pandemic 2009 H1N1 virus in place of the original M gene in the swine-origin triple reassortant H3N2 virus.
- The M gene plays a role in influenza virus infection, assembly and replication, but the significance of this change in these swine-origin trH3N2 viruses is unknown at this time.
- CDC is continuing to investigate the implications of this genetic change.
- These cases from Indiana and Pennsylvania represent the ninth and tenth reports to CDC of human infection with swine-origin trH3N2 virus since 2009, but these are the first two reports of human infection with a swine-origin trH3N2 virus with the M gene from a 2009 H1N1 virus.
- Surveillance for both seasonal and novel influenza viruses is conducted by CDC and state and local health partners year-round.
- In 2007, human infection with a novel influenza A virus became a nationally notifiable condition in the United States. Novel influenza A virus infections include all human infections with influenza A viruses that are different from currently circulating human influenza H1 and H3 viruses. These viruses include those that are subtyped as non-human in origin and those that are unsubtypeable with standard methods and reagents.

- International Health Regulation (IHR) reports were submitted for both cases per the World Health Organization reporting requirements in the event of a human infection with a novel or animal-origin influenza virus.
- Clinicians who suspect influenza virus infection in humans with recent close contact with swine, especially during times of low influenza virus circulation, should obtain a nasopharyngeal swab from the patient, place the swab in a viral transport medium, contact their state or local health department to facilitate transport and timely diagnosis at a state public health laboratory, and consider empiric neuraminidase inhibitor antiviral treatment.

Indiana Case

- A medically fragile male child with multiple co-morbidities became ill with influenza-like symptoms (fever, cough, congestion, fatigue and diarrhea) on July 23, 2011. The patient has since returned to baseline health status.
- The child was not treated with influenza antiviral medications but had received influenza vaccine in September 2010.
- The child was seen at a local emergency department on July 24, 2011. A nasopharyngeal swab specimen tested positive for influenza A (H3) and was forwarded to the Indiana State Department of Health for further testing as part of routine CDC-supported influenza surveillance.
- Testing at the Indiana State Department of Health identified suspect swine-origin triple reassortant influenza virus and the specimen was sent to CDC for further characterization.
- On August 18, 2011, the Influenza Division at CDC used PCR to determine the specimen was a suspect swine-origin triple reassortant influenza A (H3N2) virus; this was confirmed on August 19 by genetic sequencing.
- Genetic sequencing revealed reassortment between previously isolated swine-origin trH3N2 virus and the pandemic 2009 H1N1 virus; one of the eight gene segments (the "M" gene) of the trH3N2 influenza virus from this Indiana case was borrowed from the 2009 H1N1 virus.
- This reassortment has been seen in laboratory experiments, but this case is the first recognized case of human infection with swine-origin triple reassortant influenza A (H3N2) virus with the M segment gene from the pandemic 2009 H1N1 virus to date.
- An International Health Regulation (IHR) report was submitted on August 20, 2011 per the World Health Organizations reporting requirements in the event of a human infection with a novel or animal origin influenza virus infection.
- While an investigation into the source of exposure of the Indiana patient is ongoing, there is no reported direct contact between the patient and swine in this case. However, a close contact of the patient reported having swine contact.

- While more information is needed, the situation in Indiana is suggestive of possible human to human transmission of this virus and the investigation into other possible influenza infection is ongoing.

Pennsylvania Case

- A female child with a history of premature birth and mild asthma became ill with influenza-like symptoms (fever, cough and fatigue) on August 20, 2011. The patient continues to recover from this illness and is under the care of a pediatrician.
- The child was not treated with influenza antiviral medications but had received influenza vaccine in September 2010.
- The child was taken to a local hospital emergency department on August 20, 2011 where a nasopharyngeal swab and nasal wash specimen were collected.
- The nasopharyngeal swab and nasal wash specimens were forwarded to the Pennsylvania State Department of Health Bureau of Laboratories as part of routine CDC-sponsored influenza surveillance.
- On August 23, 2011, diagnostic testing of the specimens at the state laboratory indicated suspect swine-origin influenza A (H3N2). Both specimens were forwarded to CDC for further characterization.
- On August 26, 2011, the Influenza Division at CDC used genome sequencing to determine the virus was swine-origin triple reassortant influenza A (H3N2) virus with the M gene from the pandemic 2009 H1N1 virus.
- This case is the second recognized case of human infection with swine-origin triple reassortant influenza A (H3N2) virus with the M segment gene from the pandemic 2009 H1N1 virus to date (the first being the case in Indiana).
- No epidemiologic links between the two cases have been identified.
- An investigation into the source of the exposure has revealed direct contact between the patient and swine. (The patient's parent reported visiting an agricultural fair four days before the onset of symptoms.)
- Further investigation of close contacts to the child, potential additional sources of the patient's infection and ill contacts of fair exhibitors and attendees is ongoing.
- An International Health Regulation (IHR) report was submitted on August 26, 2011 per the World Health Organizations reporting requirements in the event of a human infection with a novel or animal origin influenza virus infection.

Human Infections with Swine-Origin Influenza Viruses

- Swine are susceptible to swine, avian and human influenza viruses.

- Swine flu viruses do **not** normally infect humans. However, sporadic human infections with swine flu have occurred.
- Swine-origin trH3N2 viruses were first detected in North American swine herds in the late 1990s.
- Swine trH3N2 viruses commonly circulate in pigs in North America, but only rare cases of human infections with these viruses have been detected.
- These two cases are human infections with swine-origin trH3N2 influenza virus, a virus that normally infects pigs.
- Influenza viruses are constantly changing and it's possible for two viruses to swap genes if a "host" is infected with more than one influenza virus at the same time.
- Most commonly, cases of human infection with swine-origin influenza viruses occur in people who have been in close proximity to infected pigs.
- The viruses in these two cases are different from the 2009 H1N1 virus that has been circulating in the United States since April 2009. The viruses in both of these cases have acquired the M gene from the pandemic 2009 H1N1 virus.
- Swine-origin trH3N2 virus infections in humans have also been reported from Kansas and Iowa in 2009 and from Minnesota, Wisconsin and Pennsylvania in 2010, although the viruses in these cases did not carry the M gene from the pandemic 2009 H1N1 virus.
- These two cases bring the number of human infections with swine-origin influenza viruses reported in the United States to 23 since December 2005, with ten of these now being infections with swine-origin trH3N2 viruses. However, these are the first two instances of human infection with swine-origin trH3N2 viruses that have the M gene from the pandemic 2009 H1N1 virus.
- In the past, CDC received reports of approximately one human infection with a swine influenza virus every one to two years, but in the past few years, about three to four cases have been reported per year; this increased reporting may partially be because human infection with novel influenza viruses became reportable in 2007.
- Although the vast majority of instances of human infection with animal influenza viruses do not result in human to human transmission, these cases should be fully investigated to be sure that such viruses are not spreading among humans and to limit further exposure of humans to infected animals if infected animals are identified.
- CDC publicly reports human infections with novel influenza viruses in its FluView U.S. Weekly Influenza Surveillance Report.

Acquisition of the "M" Gene into Swine-Origin trH3N2 Influenza Viruses in Humans

- Genetic sequencing of swine-origin trH3N2 influenza viruses from Indiana and Pennsylvania indicates that these viruses have acquired the "M" gene from the 2009 H1N1 virus.

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- Although reassortant viruses between swine influenza and 2009 influenza A (H1N1) have been reported in pigs, this particular genetic combination of swine influenza virus segments is unique and has not been reported previously in humans.
- The prevalence of this reassortant virus in swine is unknown.
- The M gene encodes two proteins, which play a role in the structure, replication and maturation of influenza A viruses.
- The significance of this genetic variation is uncertain.
- While the two swine-origin trH3N2 influenza viruses sequenced from Indiana and Pennsylvania are similar in that they both contain the M gene mutation, the viruses are not identical, indicating they were not acquired from a common source.
- The viruses in these two cases are resistant to amantadine and rimantadine, but are susceptible to the neuraminidase inhibitor drugs oseltamivir and zanamivir.

Swine Influenza

- Swine Influenza (swine flu) is a respiratory disease of pigs caused by type A influenza virus that regularly causes outbreaks of influenza in pigs. Swine flu viruses can cause high levels of illness and low death rates in pigs. Swine influenza viruses may circulate among swine throughout the year, but most outbreaks occur during the late fall and winter months similar to outbreaks in humans.
- There are four main influenza type A virus subtypes that have been isolated in pigs: H1N1, H1N2, H3N2, and H3N1. Most flu viruses circulating in pigs are referred to as triple reassortant viruses because these flu viruses contain genes from human, swine and avian influenza viruses.
- Swine influenza viruses are not transmitted to humans by food. You can not get swine influenza from eating pork or pork products. Eating properly handled, cooked pork and pork products is safe.
- Human infection with flu viruses from pigs are most likely to occur when people are in close proximity to infected pigs, such as in pig barns and livestock exhibits housing pigs at fairs.
- Swine flu viruses are thought to be spread from pig to pig mostly through close contact among pigs and possibly from contaminated objects moving between infected and uninfected pigs.
- Signs of swine flu in pigs can include sudden onset of fever, depression, coughing (barking), discharge from the nose or eyes, sneezing, breathing difficulties, eye redness or inflammation, and going off feed. However, some pigs infected with influenza viruses may have no symptoms or mild illness.
- For more information about swine influenza, see "Background Information on Influenza in Pigs" at <http://www.cdc.gov/flu/swineflu>.